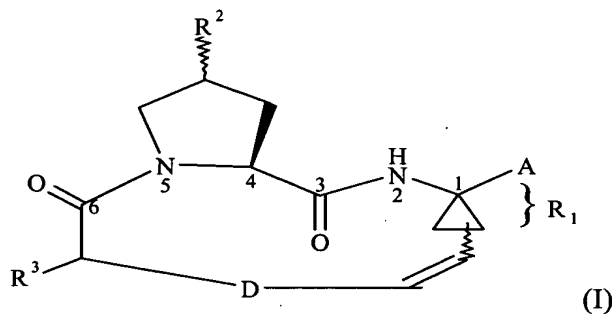


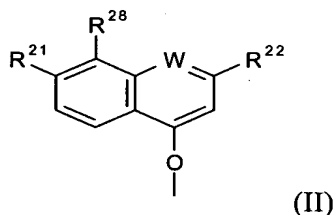
CLAIMS

1. A process for the preparation of a macrocyclic compound of formula I



wherein

R^2 is a hydroxy group, a leaving group or a group of formula II



W is CH or N,

R^{21} is H, halo, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{3-6} cycloalkoxy, hydroxy, or $N(R^{23})_2$,

wherein each R^{23} is independently H, C_{1-6} alkyl or C_{3-6} cycloalkyl;

R^{22} is H, halo, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} haloalkyl, C_{1-6} thioalkyl, C_{1-6} alkoxy, C_{3-6} cycloalkoxy, C_{2-7} alkoxyalkyl, C_{3-6} cycloalkyl, $C_{6 \text{ or } 10}$ aryl or Het, wherein Het is a five-, six-, or seven-membered saturated or unsaturated heterocycle containing from one to four heteroatoms selected from nitrogen, oxygen and sulfur;

said cycloalkyl, aryl or Het being substituted with R^{24} , wherein

R^{24} is H, halo, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} alkoxy, C_{3-6} cycloalkoxy, NO_2 , $N(R^{25})_2$, $NH-C(O)-R^{25}$; or $NH-C(O)-NH-R^{25}$, wherein each R^{25} is independently: H, C_{1-6} alkyl or C_{3-6} cycloalkyl; or

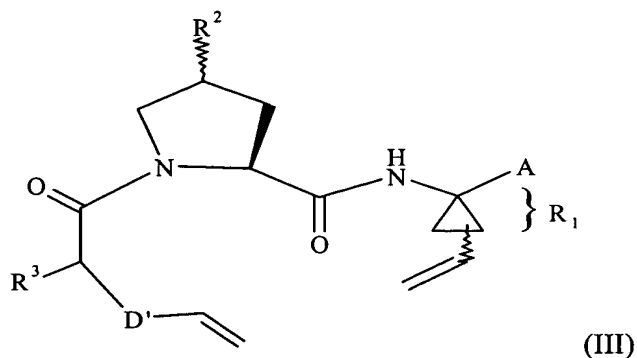
R^{24} is $NH-C(O)-OR^{26}$ wherein R^{26} is C_{1-6} alkyl or C_{3-6} cycloalkyl;

R^{28} is H, halo or C_{1-6} alkyl,

R^3 is hydroxy, NH_2 , or a group of formula $-NH-R^{31}$, wherein R^{31} is $C_{6 \text{ or } 10}$ aryl, heteroaryl, $-C(O)-R^{32}$, $-C(O)-NHR^{32}$ or $-C(O)-OR^{32}$,

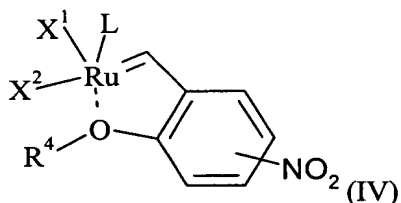
wherein R^{32} is C_{1-6} alkyl or C_{3-6} cycloalkyl;

- D is a 3 to 7-atom saturated alkylene chain; and
 A is an amide of formula $-C(O)-NH-R^5$, wherein R^5 is selected from the group consisting of: C_{1-8} alkyl, C_{3-6} cycloalkyl, $C_{6 \text{ or } 10}$ aryl, C_{7-16} aralkyl; and SO_2R^{5A} wherein R^{5A} is C_{1-8} alkyl, C_{3-7} cycloalkyl or $\{C_{1-6}$ alkyl- C_{3-7} cycloalkyl $\}$, or
 A is a carboxylic acid or a pharmaceutically acceptable salt or ester thereof; which process comprises subjecting a diene compound of formula III



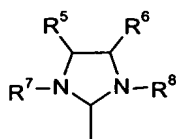
- wherein R^2 , R^3 and A are as defined hereinbefore; and
 D' represents a 3 to 7-atom saturated alkylene chain;

to a metathesis cyclization reaction in the presence of a ruthenium catalyst of formula IV:



- wherein
 X^1 and X^2 each independently represent an anionic ligand;
 L represents a neutral electron donor ligand; and
 R^4 represents a C_{1-6} alkyl, C_{2-6} alkenyl or C_{6-12} aryl- C_{1-6} alkyl group.

2. A process according to claim 1 for the preparation of a macrocyclic compound of formula I, wherein L of formula IV is a trihydrocarbylphosphine group or a group of formula



wherein

R^5 and R^6 each independently represent a hydrogen atom or a C_{1-6} alkyl, C_{2-6} alkenyl, C_{6-12} aryl or C_{6-12} aryl- C_{1-6} alkyl group; or

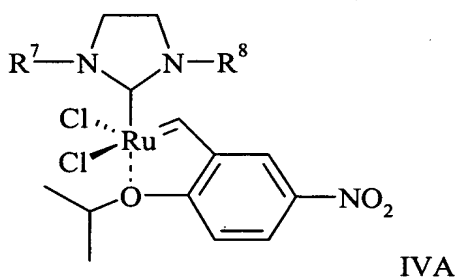
R^5 and R^6 together form a double bond; and

R^7 and R^8 each independently represent a hydrogen atom or a C_{1-6} alkyl, C_{2-6} alkenyl, C_{6-12} aryl or C_{6-12} aryl- C_{1-6} alkyl group, each optionally substituted by one, two or three groups independently selected from halogen, C_{1-6} alkyl and C_{1-6} alkoxy;

X^1 and X^2 each independently represent a halogen atom; and

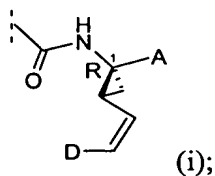
R^4 represents a C_{1-6} alkyl group.

3. A process according to claim 1 for the preparation of a macrocyclic compound of formula I, wherein the ruthenium catalyst is a compound of formula IVA



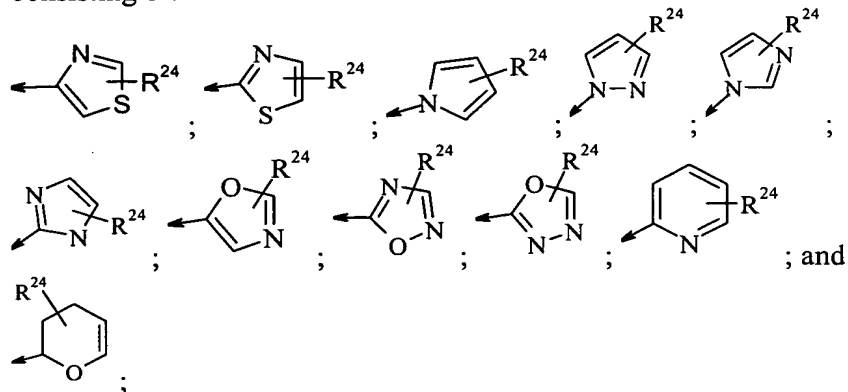
wherein R^7 and R^8 represent a mesityl group.

4. A process according to claim 1 for the preparation of a macrocyclic compound of formula I, wherein R_1 moiety is a group of formula (i)



R^2 is a group of formula II; and

W is N;
 R²¹ is H, C₁₋₆ alkyl, C₁₋₆ alkoxy, hydroxy, chloro;
 R²² is H, C₁₋₆ thioalkyl, C₁₋₆ alkoxy, phenyl or Het selected from the group consisting of:



wherein R²⁴ is H, C₁₋₆ alkyl, NH-R²⁵, NH-C(O)-R²⁵, NH-C(O)-NH-R²⁵,
 wherein each R²⁵ is independently: H, C₁₋₆ alkyl, or C₃₋₆ cycloalkyl;
 or NH-C(O)-OR²⁶, wherein R²⁶ is C₁₋₆ alkyl;

R²⁸ is H, bromine or methyl; or

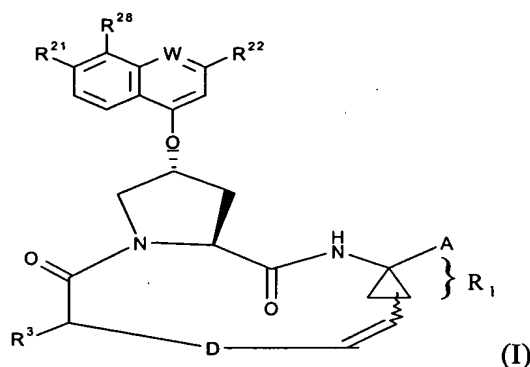
R² is a leaving group of formula -OSO₂-R²⁷, wherein R²⁷ is selected from
 p-toluy, p-bromophenyl, p-nitrophenyl, methyl, trifluoromethyl,
 perfluorobutyl and 2,2,2-trifluoroethyl.

5. A process according to claim 1 for the preparation of a macrocyclic compound of
 formula I, wherein metathesis reaction is carried out in the presence of a diluent in
 a temperature range from 40 to 120 °C.
6. A process according to claim 1 for the preparation of a macrocyclic compound of
 formula I, wherein metathesis reaction is carried out in the presence of a diluent
 selected from alkanes, aromatic hydrocarbons, and chlorinated hydrocarbons.
7. A process according to claim 1 for the preparation of a macrocyclic compound of
 formula I, wherein the molar ratio of the diene compound of formula III to catalyst
 of formula IV ranges from 1000 : 1 to 100 : 1.

8. A process according to claim 1 for the preparation of a macrocyclic compound of formula I, wherein the ratio of the diene compound of formula III to diluent ranges from 1 : 400 by weight to 1 : 25 by weight.

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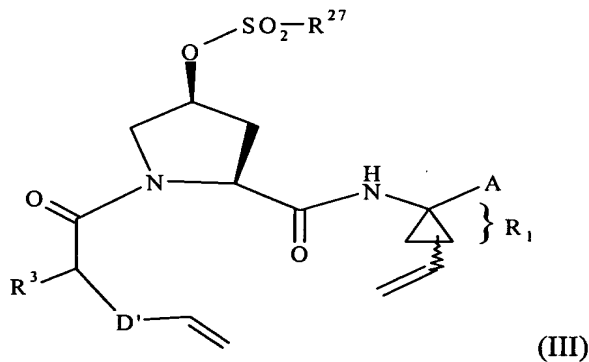
9. A process for the preparation of a macrocyclic compound of formula I



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wherein R^3 , R^{21} , R^{22} , R^{28} , W, A and D are as defined in claim 1, which comprises the following steps:

- (i) cyclizing a diene compound of formula III



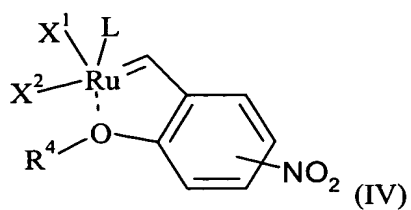
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wherein R^3 and A are as defined in claim 1, and R^{27} is selected from p-toluy, p-bromophenyl, p-nitrophenyl, methyl, trifluoromethyl, perfluorobutyl and 2,2,2-trifluoroethyl; and

D' represents a 3 to 7-atom saturated alkylene chain;

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in the presence of the ruthenium catalyst of formula IV:



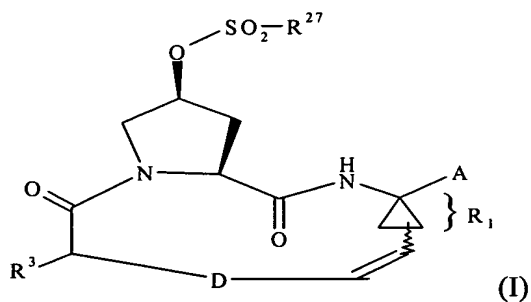
wherein

X^1 and X^2 each independently represent an anionic ligand;

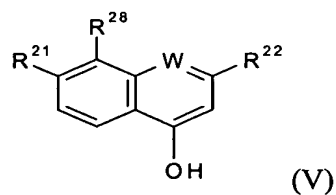
5 L represents a neutral electron donor ligand; and

R^4 represents a C_{1-6} alkyl, C_{2-6} alkenyl or C_{6-12} aryl- C_{1-6} alkyl group; and

(ii) reacting the resulting macrocyclic compound of formula I,



10 wherein A, R^3 and D are as defined in claim 1, and R^{27} is as defined above in step (i), with a compound of formula V,



15 wherein R^{21} , R^{22} , R^{28} and W are as defined in claim 1.